Docetaxel-loaded solid lipid nanoparticles as a basis for a targeted and dose-sparing personalized breast cancer treatment strategy

Dear editor

The long-term survival rate of patients with breast cancer was improved by the application of systemic adjuvant chemotherapy, although the primary breast cancer treatment strategy consists of mastectomy with lymphadenectomy and radiotherapy followed by breast reconstruction. Unfortunately, most adjuvant chemotherapeutic agents trigger major side effects. Therefore, we have read with great interest an article in the International Journal of Nanomedicine on the design of docetaxel-loaded solid lipid nanoparticles (DSNs) aimed at reducing the systemic toxicity of standardized docetaxel treatment.

Our congratulations to the authors for their clear demonstration of the reduced cytotoxicity of DSNs and significantly decreased myelosuppressive toxicity by recovering the proliferation and differentiation of bone marrow progenitor cells, while triggering more apoptosis in MCF-7 cells at a low dose compared with the commercial formula of docetaxel by an arrested cell cycle progression in the G2/M stage.

The incidence of breast cancer is high in Western European countries, ie, about 89.7 per 100,000 women. The same high incidence applies to other developed countries. For our part, we have analyzed the statistical data concerning breast cancer in the Russian Federation.

According to the statistical report by the Federal Research Institute for Health Organization and Informatics of the Ministry of Health of the Russian Federation between 2003 and 2012 (Table 1), the 10-year breast cancer incidence rates average 68.99 per 100,000 women (an average of 52,647 women annually), of which 95.1% cases were histologically verified. The average 5-year survival rate was 56.2% among women with breast cancer followed up in state and municipal cancer institutions. The average annual mortality of patients with verified breast cancer was 10.0% among individuals who were followed up in cancer institutes. Subsequently, between 2003 and 2012, about 25,697 women per year died of breast cancer in the Russian Federation.

Our investigation, as proved by time series analysis (JMP7 software), revealed that the incidence of breast cancer had been rising continually, with increasing trends from 2003 to 2012 at the same time the number of cancer deaths has been steadily decreasing (Table 1). Overall, the same trends exist for all cancer patients, in the same time.
### Table 1 Modified data from a statistical report for 2012 by the Federal Research Institute for Health Organization and Informatics of the Ministry of Health of the Russian Federation

<table>
<thead>
<tr>
<th>Statistical parameters</th>
<th>Years</th>
<th>2003</th>
<th>2004</th>
<th>2005</th>
<th>2006</th>
<th>2007</th>
<th>2008</th>
<th>2009</th>
<th>2010</th>
<th>2011</th>
<th>2012</th>
<th>10-year average ±95% confidence interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Incidence rates for breast cancer per 100,000 women</td>
<td></td>
<td>60.3</td>
<td>64.4</td>
<td>65.1</td>
<td>65.7</td>
<td>67.9</td>
<td>68.8</td>
<td>71.2</td>
<td>74.8</td>
<td>74.9</td>
<td>76.8</td>
<td>69.0</td>
</tr>
<tr>
<td>2. Histologically verified diagnosis of breast cancer (%)</td>
<td></td>
<td>93.7</td>
<td>94.0</td>
<td>94.4</td>
<td>94.4</td>
<td>95.4</td>
<td>95.2</td>
<td>95.6</td>
<td>95.7</td>
<td>96.6</td>
<td>96.3</td>
<td>95.1</td>
</tr>
<tr>
<td>3. Five-year survival of patients with breast cancer followed up in cancer institutions (%)</td>
<td></td>
<td>54.1</td>
<td>55.1</td>
<td>55.8</td>
<td>55.9</td>
<td>56.3</td>
<td>56.0</td>
<td>56.7</td>
<td>57.0</td>
<td>57.6</td>
<td>57.9</td>
<td>56.2</td>
</tr>
<tr>
<td>4. Annual mortality rate in women with verified breast cancer and followed up in cancer institutes (from all deaths due to cancer, %)</td>
<td></td>
<td>12.1</td>
<td>11.5</td>
<td>10.9</td>
<td>10.3</td>
<td>10.1</td>
<td>9.7</td>
<td>9.5</td>
<td>9.1</td>
<td>8.7</td>
<td>8.3</td>
<td>10.0</td>
</tr>
<tr>
<td>5. Patients having died of any cancer among individuals who were followed up in cancer institutes (n)</td>
<td></td>
<td>264,972</td>
<td>263,088</td>
<td>259,456</td>
<td>257,655</td>
<td>260,926</td>
<td>258,006</td>
<td>257,114</td>
<td>255,811</td>
<td>249,398</td>
<td>243,308</td>
<td>256,973.4</td>
</tr>
<tr>
<td>6. Women having died of breast cancer among individuals who were followed up in cancer institutes (n)</td>
<td></td>
<td>32,061</td>
<td>30,255</td>
<td>28,281</td>
<td>26,538</td>
<td>26,353</td>
<td>25,026</td>
<td>24,425</td>
<td>23,279</td>
<td>21,697</td>
<td>20,194</td>
<td>25,697.0</td>
</tr>
</tbody>
</table>

This phenomenon can be explained first by improvements in the Russian health care system. Government programs were set up applying new diagnostic technologies for early breast cancer screening, and preventive medical strategies were encouraged. Second, the rise in incidence of breast cancer might also be associated with gradual lifestyle changes. Many mothers in Russia decline breastfeeding and, in addition, worldwide environmental changes are reflected in an increased incidence of breast cancer, including in countries with a low prevalence of the disease.

This brief analysis demonstrates that our modern community calls for new therapeutic approaches in the treatment of breast cancer. We believe that further studies could show the application of DSNs to be a basic compound for a targeted and dose-sparing personalized breast cancer treatment strategy.

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Author contributions
All authors contributed to the discussion regarding the original study by Yuan et al., and revising the final manuscript, and agree to be accountable for all aspects of the work.

Disclosure
The authors report no conflicts of interest in this work.

References
Dear editor

As we all know, breast cancer is the most significant cause of mortality among females both in developing and developed countries recent years. In 2008, the percentage of breast cancer was 23% in total new cancer cases and death by breast cancer was 14% in total cancer death. We now know that the breast cancer incidence is high in the Russian Federation from the analysis by Danilova et al. Based on their data, Danilova et al found that incidence of breast cancer was increased yearly while the mortality had been reduced continually in Russian Federation from 2003 to 2012.

The incidence rates and mortality rates of breast cancer between developing and developed countries showed some differences. In 2008, about 50% of the breast cancer cases occurred in developing countries and the percentage of cancer deaths is 60%. While developed countries have the relative high incidence rates and the death rates have been decreasing continually. In contrast, incidence and mortality rates have been rising in many African and Asian countries such as Uganda and India. These data indicated that breast cancer patients especially those in developing countries need more efficient and affordable therapy.

Systemic adjuvant chemotherapy can improve outcomes after surgery for breast cancer patients. Unfortunately, most adjuvant chemotherapeutic agents, including docetaxel-one of the most effective adjuvant therapy drugs, cause serious side effect. Lots of efforts has been put into reducing side effects and enhancing antitumor activity, such as using nanotechnology to improve the formulations. Lipids are safe materials with good biocompatibility for drug formulations, some lipid-based formulations of anticancer drugs have been approved by the US Food and Drug Administration, such as Doxorubicin liposomal (New Drug Application (NDA) number 050718). To date, lipid-based nanoparticles have been proved to be one of the most promising drug-delivery candidates.

We prepared the docetaxel-loaded solid lipid nanoparticles (DSNs) which can significantly reduce the side-effect of docetaxel. Moreover, DSNs have lots of advantages compared with other nanoformulations, such as component safety, easier preparation, better stability, and controlled release etc that will promote its clinical application. These features make DSNs a potential economical adjuvant chemotherapy drug for breast cancer therapy with higher efficacy, especially affordable for patients in developing countries.

We appreciate Danilova et al proposed DSNs as a basic compound for a targeted and dose-sparing personalized breast cancer treatment strategy. There are a lot of problems that need to be overcome, such as large-scale production, targeting conjugation and on-demand release before DSNs' clinical use. We believe with the development of nanotechnology and pharmaceutics, the more effective docetaxel formulations based on DSNs will be developed and applied in the future.

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References


